CASE REPORT

Simultaneous presentation of pancreatic cancer in a genetically unrelated couple

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SUMMARY

Patients with pancreatic cancer tend to have a poor prognosis despite aggressive treatment, and their 5-year overall survival rate remains dismal. Several risk factors could potentially trigger the development of pancreatic cancer but many of them identified so far have been only weakly linked. Occurrence of pancreatic cancer in a husband and wife around the same time in the same household even when exposed to similar environmental factors is rare. Although familial pancreatic cancer is a known entity, pancreatic cancer in genetically unrelated married couples has not been studied. Here we present such a scenario involving one couple. In this case report, we discuss the chronological events leading to pancreatic cancer in a genetically unrelated married couple and the risk factors that may have led to cancer, in addition to exploring the possible links.

BACKGROUND

Survival in patients with pancreatic cancer remains dismal, therefore identifying the environmental risk factors that could trigger this disease is vital. Even though several pancreatic cancer risk factors have been described in the literature, few were found to be consistently associated with the development of pancreatic cancer. Often, pancreatic cancers can occur in patients without any identifiable risk factors. Since married couples reside in the same place, exposed to same environment, and are genetically unrelated, tracking their environmental exposure may help us identify the risk factors associated with the pancreatic cancer.

CASE PRESENTATION

A 66-year-old African-American man presented to his primary care physician (PCP) because of continued abdominal pain after undergoing sigmoid colectomy for diverticulitis. CT scan revealed a mass in the pancreas with possible evidence of metastasis. This was confirmed on exploratory laparotomy with biopsy of the peritoneal lesion revealing metastatic adenocarcinoma of the pancreas. The patient's medical history included hypertension, chronic back pain, hyperlipidaemia, diverticulitis and arthritis. His family history was significant: his mother had been afflicted by breast cancer and his father had had diabetes and chronic kidney disease. He had no history of smoking but drank alcohol occasionally. He had worked as a police officer for several years. He denied any occupational exposure. His medications prior to the diagnosis included valsartan/hydrochlorothiazide, statin, saw palmetto tablets, tadalafil and multivitamins. He

denied taking any herbal medications. Physical examination was non-focal. His body mass index (BMI) at presentation was 33.3 kg/m².

A 53-year-old African-American woman presented to her PCP with abdominal pain radiating to her back. CT scan of the abdomen and pelvis performed on the same day as that of her husband revealed a mass in the pancreas with evidence of multiple lesions in other organs. Subsequently, she had an endoscopic ultrasound guided biopsy and the pathology revealed pancreatic adenocarcinoma. She denied any history of weight loss or loss of appetite. Her medical history was significant for asthma and hypertension. Family history included diabetes in her mother and an unknown type of cancer in her maternal aunt and paternal grandmother. She smoked cigarettes for several years, but quit 9 months prior to her diagnosis. She denied any history of sustained alcohol consumption. Prior to marriage, her husband and she had worked in the same office for at least a year. Her medications prior to diagnosis included oestradiol, fluticasone/salmeterol inhaler, ipratropium/albuterol inhaler, lisinopril, montelukast and multivitamins. Physical examination demonstrated only mild upper abdominal tenderness. The patient's BMI was 29.5 kg/m² at diagnosis.

INVESTIGATIONS

Both patients reported in this manuscript underwent CT scan of the abdomen and pelvis, and, eventually, tissue biopsy, either by laparotomy or endoscopic ultrasound.

TREATMENT

Our manuscript is focused more on identifying the risk factors associated with pancreatic cancer than on treatment.

OUTCOME AND FOLLOW-UP

The patients and their family do not want us to report the outcome in the manuscript.

DISCUSSION

The incidence of pancreatic cancer is 12.3/100 000 men and women per year, with a death rate of 10.9 per 100 000 men and women per year. As reported in the National Comprehensive Cancer Network (NCCN) guidelines, during the year 2014, an estimated 46 420 people will be diagnosed with pancreatic cancer and 39 590 people will die secondary to it.¹ Pancreatic cancer occurs less commonly before 45 years of age, but its incidence rises sharply thereafter. Long term survival in pancreatic

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cancer is dismal, with a 5 year overall survival rate varying between 4% and 6%.¹ Over 85% of exocrine pancreatic cancers are adenocarcinomas, with other variants making up the rest.² The majority of pancreatic cancers are idiopathic in nature with the exception of a few cases where an actual risk factor could be identified. A report by Yachida *et al* in 2010, studying cancer biology in seven metastatic pancreatic patients with cancer, demonstrated that genetic alteration in normal pancreatic cells is common and the mutation leading to development of parental clone (responsible for growth of primary cancer) can take approximately one decade. Development of metastatic clone (responsible for distant metastasis) may take another 5 years, and from there an average of 2 years to death.³ However, no genetic analysis was performed in our patients due to various reasons.

This is rather an unusual presentation and, until now, to the best of our knowledge, only one such incidence has been reported, dating back to 1980. Ferguson and Watts described a case report with pancreatic cancer in a wife and husband, and attempted to explore the risk factors that lead to the development of pancreatic cancer. They noted striking dietary abnormalities including addition of coffee syrup to the ground coffee before percolation and use of excessive amounts of margarine. However, no conclusive evidence has been found yet that could link caffeine with pancreatic cancer. In addition, margarine is now no longer considered a carcinogen. Therefore, an unknown environmental risk factor was suspected in this couple.⁴

Pancreatic cancer in our patients could be coincidental, but the possibility of them exposed to or ingesting excessive amount of certain substances needs to be ruled out. Specifically, this couple lived in the same environment and worked together in the same office for at least 1 year. Association of environmental risk factors with pancreatic cancer is an area of intense debate. Arguments in favour of environmental risk factors are the presence of unequal distribution of pancreatic cancer around the world. Possible increased risk of pancreatic cancer secondary to occupational exposure to carcinogens such as chlorinated hydrocarbons, organochlorines, pesticides and formaldehyde have been described in the literature.^{5–7} N,N-Diethyl-meta-toluamide (DEET) was shown to have some neurological effects but it has not as yet been linked to any cancers.⁸

An association of dietary habits and pancreatic cancer was studied previously, however, the patients in this case series denied consuming excessive amounts of any specific substance. In one study, a reduction in pancreatic cancer with an additive effect was noted in participants who followed a strict Mediterranean diet, non-smokers, and those who consumed limited alcohol, maintained normal BMI and exercised regularly.⁹ Another study found that consuming red meat, especially when cooked at very high temperatures, increased the risk of pancreatic cancer.¹⁰ Consuming excessive vegetables and fruits has been linked to pancreatic cancer, but no conclusive evidence has been found.¹¹ Except for high fructose intake reported by one study, no association was found between carbohydrate intake and pancreatic cancer.¹²

Smoking tobacco has been consistently associated with pancreatic cancer. A pooled analysis of 12 case controlled studies demonstrated increased risk of pancreatic cancer in smokers with an OR of 1.2 in former smokers and 2.2 in current smokers. The risk increased proportionally with amount and duration of smoking.¹³ Exposure to secondhand smoke can also result in increased risk of pancreatic cancer.¹⁴ The direct effect of alcohol on the incidence of pancreatic cancer is difficult to ascertain due to the concomitant use of tobacco in many

instances but heavy alcohol consumption and chronic pancreatitis are risk factors. Pancreatic cancer-related deaths identified from cancer prevention study II found that consuming three or more drinks of liquor per day can increase the risk of pancreatic cancer, independent of smoking.¹⁵ However, pooled analysis of 10 case control studies with over 5 000 participants found insignificant association of alcohol and pancreatic cancer with ≤ 4 drinks per day but noted increased risk with ≥ 9 drinks per day.¹⁶

The couple in this report had been taking several medications and some were found to be associated with pancreatic cancer. For example, ACE inhibitor or angiotensin receptor blockers have shown a protective effect against pancreatic cancer, according to one study.¹⁷ Khurana *et al*¹⁸ demonstrated a similar outcome in patients at Veteran Affairs, after controlling for common variables. Based on a mouse model, eicosapentaenoic acid, a component of fish oil, was noted to decrease the risk of pancreatic cancer.¹⁹ However, no human studies have confirmed this finding. Use of glucosamine and chondroitin sulfate has shown a non-statistically significant reduction in the incidence of colorectal cancer.²⁰ However, in pancreatic cancer, use of glucosamine was associated with slight increased risk of mortality.²¹ Moreover, whether glucosamine/chondroitin sulfate affects the incidence of pancreatic cancer is unclear.

Naproxen was found to be effective in the prevention of urinary bladder and colon cancer.²² Naproxen can induce cell apoptosis by downregulating bcl-2 and upregulating Bax.²³ A similar outcome with reduced risk of pancreatic cancer in patients using non-steroidal anti-inflammatory drugs has been demonstrated in one study.²⁴ The effect of aspirin on pancreatic cancer demonstrated conflicting results, with some studies showing a protective effect while others found no association.^{25–28} Use of statins was associated with a non-significant reduction in risk of pancreatic cancer based on one meta-analysis.²⁹ Selenium, an antioxidant, was found to be inversely associated with the risk of pancreatic cancer but the observed association was attenuated by selenium supplementation.³⁰ However, in prostate cancer, high selenium status was linked to increased risk of high-grade tumours.³¹ Vitamin D has demonstrated reduced risk of pancreatic cancer and other cancers; therefore, its use in cancer prevention is currently being evaluated.³² Possible mechanisms include the fact that vitamin D may potentially inhibit pancreatic cancer cell proliferation, induce differentiation and promote apoptosis.^{32–33}

Other risk factors for pancreatic cancer include obesity in addition to high waist-hip ratio.^{34–35} Infections such as helicobacter pylori and hepatitis B virus in one study each, were shown to increase the risk of pancreatic cancer.^{36–37} In one study, hepatitis C viral infection was noted to increase the risk of pancreatic cancer slightly, but the effect was found to be insignificant when adjusted for other variables.³⁸

Learning points

- ▶ Pancreatic cancer is a leading cause of death and has an extremely poor prognosis.
- ▶ Since a cure for pancreatic cancer has not been found, there is an urgent need to identify its risk factors and prevent it.
- ▶ Occurrence of pancreatic cancer in genetically unrelated people living in the same household is rare.
- ▶ Studying such cases may give us a clue regarding its cause.

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